REMARKS

Applicants have amended claims 9, 14 and 19 and have added new claims 23 and 24. Upon entry of this amendment, claims 9, 14 and 16-24 will be under examination.

Support for the amended claims and new claims can be found throughout the specification. For example, support for "wherein the organ contains the ischemic reperfusion injury prevention preparation while isolated and prior to implantation" can be found at page 1, lines 9-16 and Examples 6-9. Support for "immunoregulatory activity" and "complement inhibitory activity" can be found at page 7, lines 35-45; Examples 1, 4-9; and original claims 2 and 3. Support for "non-reducing" and the non-reducing solution "SOLTRAN", which is glutathione free, can be found at page 12, lines 10-16; page 13, lines 15-22; page 15, line 44; and Examples 4 and 5. Support for "a liver" can be found at page 14, line 3. By making these amendments, applicants have chosen to focus on preferred embodiments.

The office action is discussed below.

Priority

On page 2 of the office action, the examiner objected to the specification. Applicants note that the priority information was added to the specification by the

preliminary amendment dated September 10, 2001. Applicants request withdrawal of the objection.

Written Description

Without acquiescing in the rejection, applicants submit that the amendment adding a recitation of activity moots the rejection.

Anticipation

On pages 2-3 of the office action, the examiner has repeated the rejection of the claims as being anticipated by both Ritterhaus *et al.*, U.S. Patent No. 6,193,979 and Smith *et al.*, U.S. Patent No. 6,713,606. Applicants respectfully disagree with the examiner and traverse the rejection.

Applicants reiterate that in order to reject a claim under 35 USC § 102, the examiner must demonstrate that each and every claim term is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (Rev. 2, May 2004). Claim terms are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (Rev. 2, May 2004). Claims are to be given their broadest reasonable interpretation consistent with applicants' specification. *See In re Zletz*, 13 USPQ2d 1320, 1322

(Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111(Rev. 2, May 2004).

Not only must the claim terms, as reasonably interpreted, be present, an allegedly anticipatory reference must enable the person of ordinary skill to practice the invention as claimed. Otherwise, the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Brown*, 141 USPQ 245, 249 (CCPA 1964). Applicants review below the references with these concepts in mind.

As explained previously, the Ritterhaus relates to a composition comprising complement proteins related to the complement receptor type 1 (CR1) and preferably in combination with the Lewis X antigen or the sialyl Lewis X antigen (see column 1, lines 16-25). Ritterhaus *et al.* refer to forms of soluble CR1 (sCR1), wherein the polypeptide chain contains modified glycoforms (including Le^x and sialyl Le^x) (see for example, col. 9, lines 58-66), which are <u>not intrinsically membrane-interactive</u>. The compositions of Ritterhaus *et al.* mediate binding to membranes only if a protein (*e.g.*, E-selectin), for which these glycoform modifications are ligands, is expressed in a membrane-bound form on cells. Ritterhaus does not disclose

> at least two membrane binding elements, wherein (a) at least one membrane binding element is a non-peptidic membrane binding element comprising acyl groups, and (b) at least one membrane

> binding element is a peptidic membrane binding element comprising basic amino acids, wherein the peptidic membrane binding element is bound to the non-peptidic membrane binding element and the fragment of complement receptor 1....

In contrast, the claimed methodology employs soluble derivatives that comprise at least two such binding elements and therefore intrinsically can bind to any cell membrane, and are not dependent on the presence of an up-regulated protein for binding. This allows delivery and retention of very high levels of a complement regulatory molecule to an organ.

Applicants also wish to remind the examiner that Rittershaus *et al.* disclosed a CR1 protein which was not the CR1 fragment recited in the claims, but was modified by glycoform manipulation. Such modification is not possible for SEQ ID NO:1, which differs from Ritterhaus' protein because, among other things, SEQ ID NO:1 lacks a single N-linked glycosylation site from which a sialyl Le^x structure could be attached. Thus, even if the composition of Ritterhaus *et al.* were to be retained in ischemic organs, which the examiner has not demonstrated, such a molecule could not be derived from the region of CR1 utilized in the instant invention. In sum, because Ritterhaus does not disclose the same type of molecule as is claimed, this reference cannot anticipate the claims.

Turning to Smith, this patent discloses soluble derivatives of soluble peptides that can be used according to the invention. The present claims,

however, are not solely directed to such composition or derivatives, but rather inventive methods of use for the soluble derivatives. Such claims are specifically permitted under 35 USC §§ 100(b), 101. These methods require the presence of the soluble derivative in an isolated organ. Accordingly, the invention claimed here requires the organ to be in an *ex vivo* environment, which precedes transplantation. The Smith patent does not concern organ removal to an *ex vivo* environment, and certainly all medical practitioners, as well as patients, would not consider organ removal for transplantation to be an implicit or obvious extension of other therapeutic treatments, which do not involve *ex vivo* environments. Accordingly, applicants respectfully request withdrawal of the rejection.

Obviousness

On pages 3-4 of the office action, the examiner rejected claims 9 and 18 under 35 USC § 103 over Ritterhaus and Smith. In sum, the examiner seeks to reconstruct Ritterhaus by substituting Ritterhaus' compound with the compounds of the Smith patent. The examiner, however, has provided no factually-supported rationale for performing a method that would require substituting Ritterhaus' transplant compound with the compound of the Smith patent when the Smith patent says nothing about the use of its compounds in a transplantation (*ex vivo*) environment. As stated above, organ removal for transplantation is very different from other therapeutic regimens in that organ

transplantation involves the *ex vivo* environment and the movement of an organ from one subject to another with typically a storage step in between. This complex medical procedure is not implicated in any way by the examiner's citation to the mere mention of "post-ischemic reperfusion injuries". Applicants therefore submit that the examiner has undertaken a proscribed hindsight reconstruction of the prior art, and therefore has not established a *prima facie* case of obviousness. Accordingly, applicants respectfully submit that the rejection should be withdrawn.

New Matter

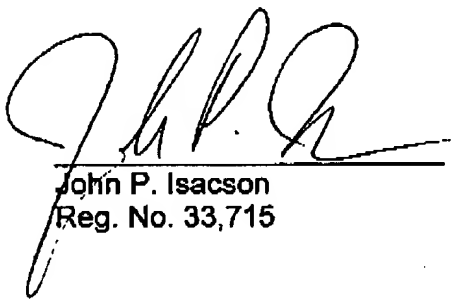
On page 7 of the office action, the examiner stated that the derivative APT 070 was "new matter," and therefore any discussion thereof was irrelevant. Applicants had cited to this derivative as evidence of unexpected results.

The examiner's invocation of "new matter" is not understood and is inapplicable here because applicants have not amended the specification to include additional discussion concerning APT 070. *See* 35 USC § 132 (stating that "[n]o amendment shall introduce new matter into the disclosure of the invention."). In any event, APT 070 is disclosed as "070" in the specification and has a sequence according to SEQ ID NO:1 and Example 1, and is also disclosed in Example 8 of the Smith patent. See the captioned application at page 19, line 9-10. Withdrawal of the rejection is therefore requested.

REQUEST

Applicants submit that the claims are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



April 13, 2006
Date

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